THE ETIOLOGY, DIAGNOSIS, AND TREATMENT OF MALIGNANT DISEASE.[1]

By FREDERIC S. DENNIS, M.D.,

OF NEW YORK,

SURGEON TO BELLEVUE AND TO ST. VINCENT'S HOSPITALS; PROFESSOR OF SURGERY IN THE BELLEVUE HOSPITAL MEDICAL COLLEGE.

IN assuming the office of the presidency, it becomes my first and pleasing duty to cordially thank the members of this association for the great honor which they have seen fit to confer upon me. It will be my aim to make this meeting a memorable one in the history of the association. The records, the discussions, and the clinical work of this organization are well known throughout the civilized world. It is, therefore, with a keen feeling of inability to instruct so many eminent men that I approach my task with much hesitation. The great prominence which the council has given this year to a discussion of the results of treatment in malignant disease has directed my attention to this subject.

In the busy pursuits of our professional work tangible results are desired. The days for speculation in fanciful theories are past, and every worker in this society believes that practical results, which can only be obtained by careful analysis and scientific study, are the only reliable helps to guide us in our search after the truth.

I have selected, therefore, a subject for discussion upon which I possess reliable and accurate data. It is a subject, too, which has never been considered in the manner in which I shall present it to you upon this occasion, and, furthermore, it is a subject the materials of which have involved many years of study and observation.

---

[1] The Presidential address delivered at the opening of the session of the American Surgical Association, of 1895.

With this brief introduction, I shall invite your attention to some clinical remarks upon malignant tumors, including a report of a series of cases which have been cured beyond the three years' limit of time, and, therefore, in all probability permanently cured, since the likelihood of return after three years' duration is infinitesimally small.

Great diversity of opinion has existed during the past few years as to the question of the curability of malignant disease. Writers upon this subject have presented a melancholy picture. Statistics have been published from time to time embracing a series of cases of carcinoma, for example; but the collection of a group of malignant tumors in which are included every kind, and affecting any structure or organ and applying a three years' limit of immunity, has never been systematically made. It matters little whether a patient has a carcinoma or sarcoma, or any other form of malignant neoplasm, the chief object of interest to him or to her is the possibility of rescue. If it can be shown that patients suffering from malignant disease can be cured by surgical interference, and at the same time the conditions necessary to effect a cure can be pointed out, brilliant results may be confidently expected in the future.

The chief difficulty in obtaining reliable statistics upon the question of permanent cures in the treatment of malignant disease lies in the fact that surgeons report cases of cure in tumors which were in reality non-malignant. In order to overcome this difficulty there should be a rule from which there is no exception. Before a tumor is classed malignant, it must be subjected to a thorough microscopical examination by a well-recognized pathologist. If this condition is not complied with the case should not be included in the list of cures. I have had many cases of malignant disease in which there was no doubt in my own mind, both from the clinical as well as from the gross appearances, yet these cases have been excluded in estimating the curability of malignant disease because a microscopical examination was wanting.

The first thing that impresses one in the study of this subject is that there are certain recognized *conditions* which give rise to malignant disease. The second thing is that apparently these same conditions exist without giving rise to malignant disease. It is, therefore, most difficult to understand why in the *one* case a carcinoma or a sarcoma develops, and in *another* case under apparently similar conditions no carcinoma or sarcoma develops. The same law which governs infection in zymotic disease is, without doubt, in operation in regard to infection in malignant disease; but the full interpretation of that law has not yet been made. The germ theory of malignant disease has not been proved to the satisfaction of the surgeon; but without doubt in due course of time light upon this important point will appear. In the present unsettled state of opinion, it is incumbent upon the surgeon to direct his attention to the *clinical* part of the question and to leave the bacteriological controversy to that domain of science. At all events, the clinical side of the question will eventually be found to harmonize with the bacteriological, and it is by pursuing the subject along these lines that an ultimate conclusion will be reached. Death is the inevitable result of malignant disease unless it is removed, and, since every one is exposed to conditions giving rise to malignant growth, it is important to inquire into the special circumstances connected with the growth and development of malignant tumors.

In presenting these cases for discussion, I do not wish it to be understood that in each case the cause which has been assigned was the *only* cause present to produce the disease.

For many years I have given the closest clinical observation to a study of the causes which give rise to the development of malignant tumors, and have read with unusual interest the discussion upon the bacteriological origin of tumors. At the present time the weight of opinion seems to be opposed to the germ theory. Clinical evidence seems to point strongly in favor of the view that changes of an inflammatory nature are responsible for the development of malignant tumors. The prominent fact is brought out in connection with a clinical study of the etiology of tumors that mechanical injury is associated with sarcoma, notably of bone; that peripheral irritation in connection with carcinoma, notably of organs and soft tissues.

Let us now examine into some cases to demonstrate the truth of the above statements. The following cases serve to illustrate the etiology of malignant tumors from *mechanical* injury:

CASE I.—I. T., aged thirty-six years, in August, 1883, was thrown from the end of a platform-car and was caught upon an iron upright, from which he was held suspended. An examination of the injured limb revealed the presence of a fracture of the lower end of the femur. Although every precaution was taken to repair the fracture, it failed to unite in the usual time. From the seat of the injury a subperiosteal sarcoma developed. In May, 1884, I amputated the limb at the hip-joint. This was just nine months from the time of the fracture.

CASE II.—J. H., aged four years, in February, 1881, received an injury to the fibula from which developed in three months a round-celled sarcoma. I amputated the limb just above the knee-joint. The patient is to-day well and with no evidence of return.

CASE III.—J. F., aged nine years, in April, 1887, received a severe blow upon the tibia, and a swelling appeared at once. In three months a tumor developed at the site of the original injury. The growth proved to be a central sarcoma of the tibia.

CASE IV.—J. N., aged sixty years, a school-teacher, in January, 1888, struck his leg violently against a school-bench, and a swelling appeared at once at the seat of injury. This tumor grew slowly, and proved to be a subperiosteal sarcoma of the tibia. In six months from the date of the injury I amputated the thigh.

CASE V.—F. F., aged ten years, in February, 1889, was struck upon the tibia by a stone. A swelling appeared, and within six months a tumor developed at the seat of the original swelling. The examination was made by Dr. Dunham while the patient was under the influence of ether, and amputation was performed as soon as the microscopical examination was announced to be subperiosteal sarcoma.

CASE VI.—M. G., aged twelve years, fell upon the back of her head while exercising upon roller skates. She struck upon the occipital bone, and a hæmatoma quickly developed. In six months following the accident a huge sarcoma developed, causing total blindness and death. The autopsy was performed by Dr. McNamara, who found a linear fracture of the skull, at the seat of which the sarcoma developed.

CASE VII.—Miss D., aged sixteen years, struck the back of her hand while exercising in the gymnasium. Over the site of injury a swelling immediately developed. The tumor was painful and grew very rapidly. I amputated the forearm, and the patient is perfectly well at the present time. A noteworthy clinical fact in connection with this case is the simultaneous development of a tubercular abscess in the hip-joint, which a week after the amputation of the forearm was opened and drained. I have seen also a second case of tubercular joint abscess in connection with sarcoma.

CASE VIII.—S. H., aged sixty-four years, struck his ilium against a desk. The pain and swelling were slight at first, but soon both became well marked. There was considerable pain upon movement of the back. Difficulty gradually increased, and soon he was unable to walk. Five months after the original injury I saw this patient with the late Dr. Sands, who confirmed the diagnosis of sarcoma. Patient died in about eleven months from the receipt of the injury, and the tumor was examined and proved to be sarcoma.

CASE IX.—A. T., aged twenty-four years, struck his thigh upon a piece of machinery. The force was considerable, and a periostitis developed over the site of the trauma of the bone. The swelling began to affect the shaft of the bone, but not the epiphysis. Amputation was performed at the hip-joint, from which the patient recovered, and at the expiration of four years was living with no evidences of return. The development of the sarcoma from the bone which had been injured and which had been the seat of a periostitis was most significant.

From a large number these nine cases have been selected to illustrate the etiology of sarcoma from traumatism. They have all a clear and unmistakable history of direct injury to the bone. In each case the original swelling was the seat of the malignant tumor, and with two exceptions within six months from the time of the injury. In each case a microscopical examination was made by a skilled microscopist, and in each case the tumor is presented with a microscopic slide. Admitting that the diagnosis was beyond doubt, and the history of the injury was based upon reliable information, the interesting question arises as to whether there is a direct relationship between the cause and the effect. It is not so difficult to understand that the injury acted as a predisposing cause to develop the sarcoma in each of these individual cases, as it is to explain the cause of the disease when it appears simultaneously in different parts of the body. In cases of multiple sarcoma it is a question whether there is a constitutional cause which gives rise to the growths, or whether infection spreads from a primary local centre. " Multiplicity of growth is not a proof of generalization of growth," and in the cases of multiple sarcoma there must be a primary local infection from which rapid dissemination of the disease takes place by the blood-vessels.

In one case of sarcoma of the thigh in which I amputated at the hip-joint there was immunity from the disease for six months. The disease returned in the forearm and spread rapidly, so that in twenty-four hours a tumor would actually develop. There was no return in the stump at the hip-joint, but in every organ and in almost every bone in the body sarcomatous infiltration occurred. If a sarcoma will grow in a few hours, is it not possible that from a local infection the multiple growths may derive their origin?

These nine cases of authentic history and certain diagnosis reveal evidence of a very strong nature in favor of the inflammatory origin of sarcoma. The proof is not so clear as regards carcinoma, but I will briefly cite a few cases to illustrate the probabilities that irritation is at least a predisposing cause to develop carcinoma.

The following cases serve to illustrate the etiology of malignant tumors and peripheral irritation:

CASE I.—Mrs. J., aged forty-six years, in May, 1881, gave birth to a living child during the seventh month of pregnancy. The child died, and the mother's breast filled with milk. The glands, however, very soon ceased to secrete milk. Two months later a small piece of skin became loose upon the top of the nipple; this scale of skin separated, and the surface underneath became irritated. A slight discharge followed, accompanied by a disagreeable itching sensation. This eczema continued for many months, and finally a lump appeared behind the eczematous nipple. I removed the breast with the tumor, which proved to be epithelioma. The disease returned in the cicatrix, and for a period of three years no less than eight operations were performed. The disease was finally arrested in the breast, and the return of the disease occurred in the brain, from which the patient died, eight years from the first appearance of the eczema.

I have seen two other cases of eczema of the nipple in which epithelioma followed. There is no doubt that the eczema seen in these cases is different from a simple eczema observed in other parts, since the usual conditions are absent, such as irritable and dry skin, overwork, anxiety, faulty innervation, nerve disorders in vessels and tissues, the uric or gouty diathesis, deficient kidney action, biliary exudation, and dyspepsia. It is also found where there is no friction and moisture, another condition so likely to develop ordinary eczema, illustrations of which are observed in the groin and perineum. Again, " Paget's disease of the nipple" is seen without the presence of any disorder of the internal organs, such as albuminuria, glycosuria, gout, and icterus. Finally, this disease does not disappear by the use of those means by which simple eczema is relieved. This eczema is a local affection at first, and by its continued irritation causes epithelial proliferation in the lactiferous ducts.

The eczema is at first a chronic affection of the skin about the nipple and the areola, and never extends deep into the tissues, since the erosion is superficial. This form of eczema occurring in women who have passed the climacteric is very likely to give rise to epithelioma, and there is no reason to suppose that the eczema is secondary to breast epithelioma, since the eczema antedates any signs of epithelioma in the ducts.

CASE IV.—Mrs. C., aged forty-seven years, was sent to me from Portland, Oregon. She suffered from an ulcer in the mouth, accompanied by enlargement of the submaxillary and sublingual glands. A microscopical examination showed the growth to be epithelioma. The patient had worn a red rubber plate of false teeth for many months. I removed the epithelioma, together with the gland.

The question which arises in reference to this case, as in other similar ones, is, Did the red rubber plate have anything to do with the development of epithelioma of the mouth? Red rubber contains vermilion. In an ordinary plate, which weighs about 288 grains, there are ninety-six grains of sulphuret of mercury. In other words, a patient wearing a red rubber plate carries in the mouth ninety-six grains of sulphuret of mercury, about two grains of which are in direct contact with the mucous membrane of the mouth ; but such sulphuret of mercury is insoluble in water, though it may eventually be converted into a soluble salt by the constituents of saliva. In consequence of this increased action of the superficial vessels, an inflammation of the mucous membrane must necessarily follow.

It is certain that the mercury in the red rubber must be a source of irritation to the mucous membrane of the mouth, and for this reason alone either a gold or aluminium plate should be substituted. In addition to the fact that red rubber contains mercury, it is also a non-conductor of heat and cold. This is an additional cause of irritation to the delicate mucous membrane of the mouth, just as a rubber shoe affects the foot. The membrane is irritated and scalded by constant presence of the red rubber plate, and while it is not a cause of epithelioma, yet this material produces a long-continued irritation, which devitalizes and deteriorates the tissues, and thus renders a soil favorable by malnutrition and by lowered vitality to the development of cancer. At all events, I have never seen epithelioma develop in the mouth of a patient who uses a gold plate, and, after careful inquiry, I have been unable to find any dentist who has seen the disease under these circumstances.

Case V.—Mrs. O., aged thirty-six years, in May, 1890, consulted me in reference to an ulcer upon her arm. She was burned when a child, and a considerable amount of cicatricial tissue was formed. At one point the scar was very tense, and at this place an ulcer developed which proved to be epithelioma. Here, again, is a tissue of low vitality continually irritated by traction and an epithelioma develops. I have also seen malignant disease arise in the cicatrix of a gunshot wound upon the face under similar conditions. These two cases illustrate the law that in poorly-nourished tissues malignant disease is likely to occur, especially when there is present a continual source of irritation.

CASE VIII.—Mr. T., aged sixty-five years, in May, 1890, consulted me on account of an ulcer situated upon the inner side of the cheek. The ulcer was microscopically examined and proved to be epithelioma. Patient states that for forty years he has carried a quid of tobacco in that spot. The irritating influences of the nicotine caused the tissues to be altered from their normal standard, and thus made a favorable nidus for infection. I have notes of three other cases in which epithelioma developed under precisely these same conditions. Here, again, in these four cases tobacco was not the cause *per se* of the epithelial cancer; but the irritation produced by the continual presence of nicotine predisposed the tissues, by lowering their vitality, to become infected.

Nicotine is, without doubt, a source of irritation to mucous surfaces. So great is the absorption of it by a mucous surface that one single drop placed upon the tongue of a cat prostrated the animal at once, and in less than eighty seconds destroyed life. There are about 331 grains of nicotine in a pound of tobacco, and five milligrammes will poison a dog in three minutes; one-eighth of a grain dropped upon the conjunctiva of a cat causes contraction of the pupil. Thus it is evident that a poison so virulent and so rapidly absorbed cannot but have an injurious effect upon the mucous membrane of the mouth, and these cases of epithelioma starting from the part of the buccal cavity in which tobacco is continually held is certainly a most significant fact. While a student in Langenbeck's clinic, in Berlin, I saw several cases of epithelioma of the cheek, and to this condition the term "American disease" was applied, because it was chiefly seen in Germany in those who chewed tobacco.

Another illustration of the law that continuous and unnatural irritation in the mouth is likely to cause epithelioma is found in the malignant growths affecting the tongue of those who nail laths. It is a custom with these mechanics to introduce into the mouth lath-nails and to push them out by the tip of the tongue as fast as they can be used. An expert will take into his mouth and push out of it with the tip of the tongue, at a low estimate, several thousand nails per diem. This irritation continued day after day has been followed by cancer. Recently two other cases of this kind have come under my personal observation. Here, again, I do not believe that the contact of the nails with the tongue directly caused the cancer; but the continued irritation lowered the vitality of the soft parts so as to render the tissues susceptible to infection. Other illustrations of this law, that continued and unnatural irritation is likely to predispose the tissues to infection, is seen in the irritation produced by soot in chimney-sweep's cancer, also in the irritation produced by a clay pipe, which by its adhesive qualities tears off from time to time the thin cuticle from the lip; and, again, by the irritation caused by the continual pressure of the spring of a pair of eye-glasses, two illustrations of which have recently come under my notice.

The cases reported by Dr. Gerster of epithelioma of the rectum in patients who were in the habit of using the nozzle of an injection syringe in such a manner as to daily bruise or lacerate the mucous membrane of the rectum, is another illustration of the same law. The lacerated cervix is still another good example of irritation in poorly nourished tissues causing epithelioma. Still another illustration is seen in epithelioma from a chronic ulcer of the leg.

The following cases serve to illustrate the etiology of malignant tumors from *sinus irritation:*

CASE XV.—Mrs. E. P., aged forty-eight years, in May, 1886, sustained a compound fracture of the tibia. The bone united, but a limited area of necrosis followed. From the superficial surface of the limb a small sinus led down to the necrosed bone. This sinus was lined with a pyogenic membrane and discharged thin ichorous pus. After many months a typical epithelioma developed at the mouth of the sinus. The tumor was examined microscopically and found to be epithelioma.

This case is a good illustration of the law that a discharging sinus is a source of great danger to the patient, since the continual irritation induced by the acrid pus led to the development of true epithelioma. The case shows the great danger of allowing a sinus to remain without performing an operation for its radical cure.

Case XVI.—J. T., aged forty years, in 1880 was shot in the shoulder-joint; the wound healed, leaving a small sinus which led down into the joint. The sinus remained open for many months, and at its mouth a typical epithelioma developed. The causes in this case which produced the epithelioma are identical with those just mentioned in the preceding case, and further serve to emphasize the dangers that attend a sinus which is left by the surgeon unhealed.

To reiterate what has been already said, these nine cases of sarcoma serve to forcibly illustrate the law that sarcoma of the bone is associated with injury, but that every injury of bone is not followed by sarcoma. These sixteen cases of cancer serve also to illustrate the law that this disease is associated with irritation, but that every irritation is not followed by carcinoma. The same law is present in epithelioma of the alimentary canal, since cancer is usually found in those places where there is a constriction, as in the lips, pyloric end of the stomach, ileo-cæcal valve, and rectum. In other words, there must be present a predisposition in order to develop the disease. Finally, these cases of cancer which were developed from sinus irritation and from indolent ulcers point to the same etiological law.

The question as to the etiology of tumors has been greatly simplified within the past few years, since pathologists have been able to exclude many growths that were formerly considered under the head of tumors. These growths are now included under infections. Among this group may be mentioned granuloma, tubercle, leprosy, gumma, glanders, and actinomycosis. Hydatid cysts have been eliminated from the original group of tumors, so that in reality a tumor has at the present day a most restricted meaning.

The theory of Cohnheim, that tumors arise from proliferation of embryonic cells which were displaced during fœtal life and which rapidly multiply in consequence of some exciting cause, cannot be rejected. Any attempt to explain tumor-formation except from vestiges and rests seems futile.

The theory of parasitic origin of certain tumors has been brought into prominence of late. The demodex in the skin and the coccidium in the intestine are examples illustrating the parasitic causes of tumors. In support of the parasitic origin of cancer, it is maintained that the germs gain admittance into those glands which are in direct communication with the external atmosphere or through the medium of the intestinal gases. The mammary glands, the stomach, and rectum are the organs most frequently infected by cancer, and the entrance of the parasites is explained in the manner just described.

The frequency of epithelioma of the cervix as contrasted with the rarity of this disease affecting the uterus; the infrequency of epithelioma affecting the prostate as compared with the prepuce; the frequency of the disease affecting the lips as compared with the œsophags, uare among the illustrations in support of the parasitic origin of cancer.

Among recent writers there has been a tendency to disregard the influence of injury in the development of tumors; but these twenty-five or more cases already mentioned in this paper seem to point strongly to the view that sarcoma at least is the result of cell changes due to some kind of inflammation induced by injury, and that cancer in all probability is likewise the result of some peculiar inflammation produced by continual irritation. The clinical evidence is such that the surgeon cannot disregard the strong arguments in favor of the reversion to primary cells, and if this theory is accepted the local origin of tumors seems evident. The general infection spreads from a local one, and the early and radical removal of the primary focus ought to prevent the widespread dissemination of malignant disease. As a matter of fact, the results which will presently be given seem to point to the conclusion that malignant disease is at the outset the result of local infection, and the early and complete removal of it will bring about a permanent cure.

From a careful clinical study of these cases of malignant tumors, there are some lessons which should be forcibly impressed. The first is that injury or irritation apparently is concerned in the development of malignant disease; whether these agents act as predisposing or exciting causes time only will determine. The second lesson is that all traumatisms of bone should be treated upon sound principles of surgery. The third lesson is that every unnatural irritation affecting integument or mucous membrane should be removed. In fact, the writer would go even further, and strongly recommend the removal of moles, especially those in which hairs are embedded, since these foci are often the starting-points of malignant ulcers. I have removed a large number of these moles, and in many of them a true sarcomatous structure has been found. I have here for examination a beautiful specimen of a mole apparently innocent from a clinical point of view, but which has pathologically undergone sarcomatous degeneration. It was removed for cosmetic effects, and was not considered malignant at the time.

Papillomata and warts and localized scales of psoriasis, with no tendency to heal, should be removed. The retained testicle in the inguinal canal is also another condition giving rise to degeneration which leads to true epithelioma.

These clinical facts, thus cursorily reviewed, seem to present certain questions for discussion.

(1) Has traumatism or irritation anything to do with the etiology of malignant tumors?

(2) If so, what is the relation which the cause bears to the effect?

(3) If not, how can the cases which have been reported in this paper be explained?

(4) If it is admitted that traumatism or irritation, separately or together, bear etiological relations to these tumors, how can the presence of these malignant tumors in the absence of these agencies be explained?

(5) If the theory that traumatism or irritation can develop a malignant tumor, does not the acceptance of that theory demonstrate the purely local origin of these neoplasms?

(6) Do not the cases operated upon early demonstrate the correctness of the theory that by the removal of the local infection constitutional infection can be avoided?

The *diagnosis* of malignant disease is at the present time the most important part of our subject. When the knowledge is obtained in regard to the cause and prevention of malignant disease, the second part of our subject, which involves the diagnosis, will have little interest in our discussions. In the present state of our knowledge, however, diagnosis and treatment are subjects of transcendent importance because the surgeon is confronted upon every side by the presence of malignant disease. Delay at arriving at a positive diagnosis of malignant disease is equivalent in most cases to death. The earlier a positive decision is arrived at the more certain are the prospects of cure. To this proposition all will assent; but the great difficulty which confronts the surgeon is, how can an early diagnosis be made? The duration of the growth or its rapidity are important points; but they are not always to be relied upon as infallible. For example, the writer has observed several cases of the most malignant variety of sarcoma, which, on account of the anatomical position or owing to the presence of a dense capsule, remained dormant and innocent for many years. One sarcoma of the neck, the most malignant in the list, remained in quiescence for a period of twelve years, though it had assumed the size of an orange. Complete and permanent recovery followed the operation for its removal.

Time of duration and rapidity of growth, therefore, while usually affording strong evidence in favor of malignancy, may, on the other hand, mislead in exceptional cases. Besides these two clinical facts, the age of the patient must always be considered in arriving at an early diagnosis of malignancy. As a rule, to which, of course, there are notable exceptions, carcinoma is not likely to appear before forty-five years of age. I have seen, however, cancer in a young child, and have operated on a patient over eighty years on account of the same disease; but these are to be considered as surgical curiosities.

In regard to sarcoma, the line of demarcation is not so clearly drawn. It may be said, with a fair degree of accuracy, that sarcoma appears under forty-five years of age, and that sarcoma is the characteristic malignant tumor of early life.

A certain value can also be attached to heredity. In a general summary of all cases reported upon statistics show that about 4 per cent. of the cases of malignant disease are associated with a history of heredity.

The seat of malignant tumors furnishes some knowledge as to the character of the neoplasm. For example, the primary malignant disease of bone is sarcoma, since carcinoma rarely, if ever, affects bone except as a secondary deposit. Hence, any primary malignant disease of the osseous tissue is presumably sarcoma, while, if secondary, it is in all probability carcinoma. The gross appearance of malignant tumors is characteristic. The dusky hue to the skin, the dilatation of veins over the surface, the great tendency to ulceration, the subcutaneous hemorrhagic extravasation, are points seldom seen in any other tumors except the malignant.

The consistence of a growth and the local temperature are important factors in arriving at an early diagnosis. Malignant tumors, as a rule, are firm and hard unless the growth is cystic, in which case the fluid is generally bloody and gives to the tumor a sense of fluctuation. The temperature of the part is not elevated unless there is superinduced some acute inflammatory attack. Abscesses, on the other hand, are attended by elevation of temperature, which is most striking as compared with malignant tumors. In abscess there is also pyrexia and a zone of induration which are characteristic.

The presence of pain and cachexia are also important points in connection with the early diagnosis of malignant disease. It is not only the presence of pain, but the character of the pain that must be noted. With the exception of the colloid variety of cancer, pain is present in all varieties of malignant disease. As colloid cancer is seldom situated at points amenable to surgical operation, this exception is one that is easily remembered. On the other hand, pain is absent from benign growths unless some inflammatory process has become associated with the neoplasm, and under these circumstances the pain is readily explained. Pain may also be present in a benign tumor if the nerve is included in the tumor.

It follows, therefore, that the presence of pain is of diagnostic value. In regard to the character of the pain there are some points to consider: in malignant disease the pain is not continuous; but intermittent. It is also sharp, lancinating, and darting, and it becomes more severe as the tumor develops. Finally, the pain is not increased by the manipulation of the tumor itself by the surgeon.

The cachexia of malignant disease is uniformly present sooner or later, but it is a symptom observed late in the history of the disease, and it is only in exceptional cases that its presence is of any early diagnostic value. In certain very rapidly developing growths the cachexia may appear as one of the early symptoms, but it is not a condition that affords any early information to the surgeon, no matter how soon it may appear, because its presence at any time indicates that the growth has advanced a long way in its local history.

Information derived from the harpoon is the most valuable, since it is positive. This method of diagnosticating the character of any tumor is applicable to all growths situated outside of the great cavities of the body. In exceptional cases, however, this method of early diagnosis can be employed in certain growths having their origin from the interior of the body. The method consists in thrusting a small needle protected by a canula into the interior of the tumor, and then by a rotary movement of the needle to entangle some of the tissue into the point, which is made like a harpoon. The tissue can then be examined microscopically and a positive diagnosis established. The surgeon must bear in mind that this trivial operation may occasionally excite inflammatory action in the tumor.

The *prognosis* in malignant disease depends upon many factors. It consequently has many variations. I am a firm believer in the local origin of all malignant neoplasms, although there are exceptional cases in which, I frankly admit, my belief is shaken, but only because I fail to find the exciting cause. From the local infection the disease may become constitutional. It is only when a malignant tumor is considered as a local infection that any hope can be entertained as to a complete cure. In the first list of cases reported where mechanical injury was pointed out as the etiological factor in the production of sarcoma, the prognosis depended upon early recognition of the disease and a prompt operation at a point far distant from the seat of the growth.

In the cases of Paget's disease of the nipple, the eczema should be treated at once according to the principles of antiseptic surgery. The earlier the treatment is adopted and the efficiency of the means employed determine the prognosis.

The question which most influences the prognosis in this form of malignant disease is whether the entire breast should be excised or only a portion of it, including, of course, the nipple. I am aware that surgeons advocate the latter operation, but at the same time they insist upon carefully watching the breast from time to time with a view to repeating the operation of partial excision if occasion arises, or at any subsequent period of removing the entire gland.

It is claimed that the primary removal of the breast is too serious an operation on account of an eczema possessing the characteristic features that have been described. I feel very certain that a radical operation is indicated in Paget's disease of the nipple, because it invariably leads to true epithelioma if not arrested, and a study of the cases of epithelioma from a clinical point of view demonstrates clearly the fact that it is a disease that is too dangerous to be left to partial excision. The prognosis in this affection depends upon the complete removal of the entire breast and even the pectoral fascia and the lymphatics, extending into the axilla. Any operation of less magnitude is not sufficiently radical to render the patient safe. I have found in a study of these cases that failure to remove the entire gland was soon followed by a recurrence, the prevention of which might have been averted by a thoroughly radical operation at the start. The comparative safety of removal of the breast is an argument strongly in favor of its adoption in these cases, and the prognosis in Paget's disease depends upon the question of complete or partial excision of the breast.

If the mortality of the two operations be compared,—viz., entire removal of the breast and a partial excision of the gland, —the difference will hardly be appreciable; but the question of return after the two operations is so different that the wisdom of the radical operation is apparent. The removal of the pectoral fascia occupies but a few seconds and does not add to the severity of the operation; but inasmuch as the fascia itself is often the seat of infection, and this, too, when unrecognized by the naked eye, but proved by microscopical examination, it seems wise to remove this possible source of infection. The lymphatics can easily be dissected up and torn carefully away by leaving the axillary angle of the gland intact until the end of the operation. This makes the prospects of the patient most favorable; anything less renders the prognosis extremely doubtful.

These are the means at the surgeon's command to early diagnosticate and to prognosticate in malignant tumors. The application of these fixed principles explain the reasons which influenced largely the success in arriving at the results to be presently recorded.

The next thing that has materially aided in bringing about these results has been the execution of a thoroughly radical operation. This brings us to the third part of our subject,—viz., the *treatment* of malignant disease.

For many years the writer has been collecting data for the purpose of arriving at some conclusion as to the value of operative interference. Every case has a carefully prepared history, which was taken at the time of the operation. Every specimen has been thoroughly examined by a well-known microscopist. Each tumor is preserved as well as a slide from the original growth itself. The histories, the slides, the original tumors are all here for examination, and at the clinic I shall exhibit some of the patients. The names of the surgeons who were present at each operation are also recorded. Finally, no patient is admitted in the list whose cure has not been at least for three full years, and whose complete history from the beginning down to the present time is not known. The amount of labor necessary to keep these records complete for so many years can hardly be estimated. The writer desires in this connection to urge upon the members of the association the great importance of keeping the histories, the microscopical examinations, the tumors, as well as a record of the patient's welfare from time to time. Unless this is done, no reliable information upon which to base statistics can be obtained. When this information is furnished, surgeons can very soon arrive at some positive knowledge in regard to the prognosis in the treatment of malignant disease. The writer with great humility presents these facts, since he hesitates to review the valuable work of surgeons whose reputation, skill, and knowledge are of world-wide repute.

To pass in review the work of Butlin, Williams, and Gross, not omitting the individual members of this distinguished association, is a task which any surgeon might assume with a deep sense of responsibility.

This contribution, therefore, is offered only with a desire to search after the truth. The writer also in presenting these carefully prepared facts disclaims any personal superiority in regard to operative technique, and frankly admits that certain fortuitous circumstances have attended his labors. How, then, are these results to be explained? Why are they so much better than those which have been hitherto published? What course should a surgeon take to insure the same or better results? These questions teem with profound interest to every practical surgeon. They are questions, too, that vitally concern each one of us, because the next victim to fall may be in our own circle. The medical man as well as the laity is deeply and practically concerned in these momentous issues.

The term radical treatment is susceptible of a wide range of meaning, since a radical operation to some is to others an inadequate one. An amputation may be considered radical and yet at the same time be insufficient. A sarcoma of the external malleolus requires more than amputation of the leg, since the popliteal glands are often very early affected, and, therefore, amputation of the leg is clearly inadequate. In a case of sarcoma of the external malleolus the writer has performed an amputation above the condyles of the femur. This great sacrifice was made for the express purpose of not only removing the entire bone affected, but also to insure complete extirpation of the popliteal glands. Ten years ago I adopted this method in a case of round-celled sarcoma of the external malleolus. The tumor was examined by Professor Welch, of the Johns Hopkins University, and pronounced by him as most malignant. The young man is alive and well to-day, and the tumor is here for inspection and microscopical examination.

Recently I have seen a case in which, six months ago, a surgeon excised a sarcoma from the lower end of the fibula. At the present time a large sarcoma is situated at the site of the original small tumor, and the popliteal glands are enormously enlarged, and the disease has even invaded the inguinal glands. In this case, an exact counterpart of the one just referred to, it is nearly certain that early amputation just above the condyle would have prevented a local and a regionary recurrence and death itself, for this is inevitable within a few months from now, or within a year from the time of the first inadequate operation. It may seem absurd to sacrifice so much of the body for so insignificant a growth, yet clinical history repeats itself over and over again that death is the alternative unless radical operation is boldly resorted to as a curative measure.

In performing a so-called radical operation for the removal of malignant disease, it is often a question as to how much glandular tissue it is necessary to dissect out from the adjacent tissues, and especially what particular glands require removal. In certain cases it is wholly unnecessary to extirpate some near-lying and large glands and omit the small chain of lymphatics which shoot off directly from the infected area. In epithelioma of the lip there is situated near the angle of the jaw a gland which is in connection with the labial glands. This small gland should be dissected out even though the larger and submaxillary gland beneath the jaw is apparently free from infection. The neglect to do this is often the cause of a recurrence of the cancer of the lip, even though the submaxillary gland has been extirpated. At my suggestion, Professor Gerrish has made a unique and beautiful set of plates for an article on the surgery of the lymphatic system, in which is shown the direct line of infection from any given point in the body. An examination of this chart at once reveals the points of attack that the surgeon should make after the removal of the malignant neoplasm has been effected.

At this juncture another question arises of great importance. If a radical operation is performed and recurrence takes place, is there any prospect of permanent cure by repeated operation? To this proposition I reply that operations should never be abandoned as long as the growth can be removed, provided only the metastasis has not invaded the internal organs. This suggestion has reference not only to mere prolongation of life and the amelioration of physical suffering, but it also has a direct bearing upon the ultimate and permanent cure. There are some good examples illustrating this law in some of the older works of surgery. Dr. Valentine Mott operated fifteen times in one case of sarcoma during a period stretching over twenty-three years, and Gross operated twenty-three times on a case of sarcoma covering a period of four years. The writer has removed from the same patient an axillary sarcoma, afterwards the breast, then, later, several sarcomatous glands in the inguinal region. It is now over three years since any recurrence has taken place, and the patient seems perfectly free from a return and enjoys most excellent health. A failure to operate on any of the tumors would have abandoned the patient to certain death. Repeated operation in different parts of the body has at last rescued this unfortunate patient and has placed her beyond the probable chances of death from sarcoma. In one case over two hundred individual carcinomatous tumors have been removed, and the patient is apparently free from the disease at present.

In regard to the final proposition as to the course which every surgeon should adopt to insure the best results.

The surgeon, in assuming the care of a patient with malignant disease, should apprise the friends, but not the patient, of the real dangers. It is well also to refuse to take all the steps necessary to arrive at a correct diagnosis unless assurances are given by the friends that the patient will be persuaded to abide by the result. For example, it often happens that after using the harpoon a fungous growth starts up immediately, and the patient becomes dissatisfied and abandons the surgeon to take the advice of some charlatan or quack. The harpoon should not be used unless there is a distinct understanding that if the result of the examination demonstrates the presence of malignant disease, that the permission will not be withheld to perform a radical operation.

In studying the nature and history of malignant disease, the only safety lies in early diagnosis, in a radical operation and in a repetition of the operation if necessary. The mere statement of such a proposition is of no value unless the truth of it can be proven beyond all peradventure.

The treatment of malignant disease by the injection of the toxines of erysipelas, as practised by Dr. Coley, deserves more than a passing notice. The writer would respectfully refer the members of the association to his interesting monograph upon that subject. The results of treatment by operative interference are only considered upon this occasion.

The treatment by methods based upon the same principles as are employed by Pasteur in inoculation for the cure of hydrophobia have not yet been sufficiently tested to warrant any consideration of the subject in the present paper.

In sarcoma of the *glands* statistics are very meagre. Butlin reports that he fails to discover a single case of permanent recovery after operation for the removal of sarcoma of glands.

The writer has had twelve cases of sarcoma of glands, the subsequent histories of which are all known. Recovery has occurred in every case but one, thus giving 91⅔ per cent. of permanent cures beyond the three years' limit of time. In these twelve successful and permanently cured cases of sarcoma of the glands there were some which were very large. In two the tumors involved the neck, one of which was larger than a child's head, necessitating a deep and dangerous dissection which exposed the large cervical vessels. In another case the tumor was situated about the femoral, and in another about the popliteal vessels. Some of the tumors were removed in the presence of alarming hæmorrhage, and involved a most formidable operation.

In regard to sarcoma of bone, Butlin reports 78 cases of subperiosteal sarcoma, of which the results in 28 cases are unknown, and in 6 more the patients had not reached the three years' limit of time, which leaves 44 cases in which the full subsequent histories are known. Of these 44 cases 14 died of the operation and 29 from recurrences, which leaves but one permanent cure in the 44 cases. There are thus 78 cases in which operation was performed, 14 of which died from the immediate effects of the operation, which gives 18 per cent. of mortality, and of the 44 cases whose full subsequent histories are known, there was but one permanent cure, or 2 per cent.

In periosteal round-celled sarcoma of *bone* Gross estimated the duration of life at eighteen months, and of 6 cases operated upon, only 1 remained well without local recurrence, thus giving only about 17 per cent. of permanent cures.

The writer reports 21 cases of subperiosteal sarcoma of bone in which an operation was performed, one of which, an amputation of the hip-joint, died from the immediate effects of the operation. This gives 5 per cent. mortality for the operation. The histories of 4 are unknown.

In a summary of the 17 cases of subperiosteal sarcoma in which the results are known, there are 3 deaths, 1 of which has just been referred to as a result of shock, and 14 cures beyond the three years' limit of time, which gives 82 per cent. of permanent cures. This is in marked contrast to Butlin's statistics, which record only 2 per cent.; or the more recent statistics of Gross of 17 per cent. of permanent cures.

Of central sarcoma Butlin has collected 82 cases treated by operation, of which 23 cases died from the immediate effects of the operation, thus giving a mortality of 28 per cent. Five died from recurrences; and only 10 patients were known to be alive at the end of a year, and some of the 10 after two or more years. But, of course, here there are no definite statistics.

In Warren's book on "Surgical Pathology," he reports from Gross 34 cases of central sarcoma of bone, of which 3 died without operation, and of the 31 operated upon, 5 died from the immediate effects of the operation, giving a mortality of 16 per cent. Six cases died from recurrence and 2 had not reached the three years' limit of time; there are, therefore, 18 cases still alive. Of the 31 cases operated upon 2 had not reached the three years' limit of time, which leaves 29 cases whose subsequent histories are known. Of these 18 were permanently cured, which gives us 62 per cent. The writer has had only one case of central sarcoma. This patient was operated upon and recovered and is still alive, after ten years from the date of the amputation.

Butlin describes excision for removal of sarcoma affecting bone. Such an operation is manifestly ineffectual and does not deserve a moment's consideration. In all of my 14 cases of recovery dating back over three years, the limb, with one exception, was removed so as to include the entire bone affected. Any operation short of this radical one is sure to be followed by a return. It seems a terrible sacrifice to remove the thigh at the hip-joint for a sarcoma involving the condyles, or lower third of the shaft of the thigh; or the leg above the knee-joint for a sarcoma affecting the malleolus; but these 14 cases prove the necessity, and the cases of excision or partial amputation through the bone, collected by Butlin, prove the utter uselessness of any operative measures of less radical character.

In epithelioma of the face, Butlin, from many sources, collected 206 cases. Operation was performed with 21 deaths, or a mortality of 10 per cent. There are 59 cases where subsequent histories were unknown, and of the remaining 147 cases, 25 of them had not yet reached the three years' limit of time, leaving 122 whose subsequent histories are known. Of these 21 died during treatment, and in 51 cases there was a recurrence of the disease; the remaining 50 were permanently cured. There are, therefore, 122 cases in which the history is known, of which 50 were cured, giving a percentage of permanent cures of about 41 per cent.

The writer has operated upon 8 cases of epithelioma of the face, with no mortality so far as the operation itself is concerned. In these 8 cases the subsequent histories are all known. In 1 the patient died after many local recurrences, in which more than 30 operations were performed, extending over a period of twelve years. Two died from a return of the disease within three years. The remaining 5 were permanently cured, which gives 62 per cent. of permanent recoveries. There are several cases in which recovery from the operation has taken place and in which as yet no recurrences, either local or regionary, have occurred; but these cases unfortunately have not yet reached the three years' standard, and, therefore, cannot be counted at present. There are also a large number in which the microscopical evidence is wanting, and, therefore, the cases are rejected.

In carcinoma of genitals, tongue, lips, etc., the number of each is too small upon which to base any statistics. Suffice to say, that among the cancers affecting these organs and structures there are cases of permanent cure.

Let us now turn to the consideration of the treatment of carcinoma. The necessity of an investigation of carcinoma can be estimated, when it is considered that in England alone there are 7000 deaths annually from cancer, and that there are 30,000 patients suffering at all times in that country from this affection.

The mere fact that cancer causes more deaths in the United States in one year than the sum-total of deaths due to erysipelas, tetanus, hydrophobia, lightning, typhlitis, gunshot-wounds, joint disease, together with other well-known surgical affections, conveys at once an idea of the wide dimensions of our subject. Cancer causes nearly half as many deaths in one year in the United States as are caused by accidents and injuries of all kinds and descriptions.

Dr. Billings has demonstrated by statistics that carcinoma is a disease which is slowly increasing, and that it is the cause of a larger proportion of deaths in nations which have reached the highest state of civilization. For example, in the United States in one year there were over 13,000 deaths from cancer, of which there were twice as many deaths among females as among males. There are over 14,000 people in the United States dying each year from cancer.

In cancer of the breast Halsted published a monograph in which he based his 6 per cent. of local recurrences on the 50 cases which he reported in 1894; but of these 50 cases the results of 5 he records as unknown, and 25 of them he reports not having reached the three years' limit of time. There are, therefore, only 20 cases instead of 50 that could be utilized at the time of his publication in estimating the local and regionary recurrences. In the 20 cases of which he can speak with authority, 18 of these died before the three years' limit was reached, leaving only 2 in which it can be said at the time of the publication of his paper that recovery took place according to the generally accepted standard of the three years. Halsted's figures, therefore, show 10 per cent. of permanent cures and 15 per cent. of local recurrence, since in the 20 cases there were 3 local recurrences.

Halsted has not published the work of American surgeons in his table, and there are several men in this country whose published results are much better, with one exception, than all of those recorded as the work of foreign surgeons. The high percentage of permanent cures is much more important than a low percentage of local recurrences, since the permanent cures include the regionary and local recurrences. Halsted's statement that "the efficiency of an operation is measured truer in terms of local recurrence than of ultimate cure" needs a transposition, which would read that "the efficiency of an operation is measured in terms of no mortality in the operation and permanent cure in the ultimate result."

The writer has had 116 cases of tumors of the breast, of which 19 were not operated upon, leaving 97 cases in which the breast was amputated. In the 97 cases of amputation there was but 1 death, thus giving a mortality of a little over 1 per cent. The 1 fatal case was due to the presence of hæmatophilia, and is a death that might have occurred in connection with any other operation, no matter how insignificant in character. This death can, therefore, with propriety be excluded as far as bearing upon the mortality of this special operation, and, if so, there is an unbroken series of 96 consecutive operations without a death. In addition to the reduction of the mortality of the operation from as high as 23 per cent., recorded by Billroth, to a cipher, there was no case of pyæmia, septicæmia, erysipelas, or abscess.

Of the 97 cases of amputation of the breast 23 cases of sarcoma and other tumors than cancer must be eliminated in order to compute the percentage of permanent cures of pure carcinoma of the breast. Of the 74 cases of pure carcinoma of the breast, the subsequent histories of 41 are known; 3 of these have not reached the three years' limit of time (although they are still alive and free from the disease); there remain 38 cases, therefore, of pure carcinoma of the breast in which the full subsequent histories are known. In these 38 cases there are 17 cases in which a permanent recovery has taken place. This gives 45 per cent. of permanent cures. Among these 38 cases whose histories are known there were but two local recurrences, which gives but a little over 5 per cent. of local recurrences.

Since the publication of the writer's last statistics, in 1891, he has had 15 cases of pure carcinoma of the breast, with no mortality from the operation itself. Of these 15 cases, 1 died several weeks following the operation from hæmatophilia, in which the major joints were filled with blood and the greater part of the body was affected with subcutaneous hæmorrhages. Two of the 15 cases have not yet reached the three years' limit of time. There are, therefore, 13 cases in which the full subsequent histories are known; 2 of these died from a recurrence of the disease and 1 from hæmatophilia, as stated above, and the remaining 10 have passed the three years' limit of time. This gives 77 per cent. of permanent cures in cancer of the breast in the last 15 consecutive cases.

The reason why these radical operations have not been hitherto employed in amputation of the breast lies in the fact of the mortality of the operation, since Gross reports 10 per cent. mortality; Sir Joseph Lister, 8 per cent.; Butlin, 7 per cent.; Fischer, 20 per cent.; Esmarch, 10 per cent.; Küster, 14 per cent.; Billroth, 15 per cent.; and again Billroth, in a previous list, 23 per cent. In my list of cases of amputation for all kinds of tumors of the breast, the mortality of the operation is less than 2 per cent. This mortality includes the results of radical operation. In Weir's list the mortality is reduced to zero. If this represents the mortality, there is no longer any reason for surgeons to offer the dangers of the mortality of the operation as an excuse for refusing radical operation, since it is in those cases in which a most complete operation has been performed that permanent recoveries follow.

In sarcoma of the *breast* statistics are very meagre. Butlin in his book gives no results either as to mortality or as to permanent recoveries.

Williams in his book reports 10 cases of sarcoma of the breast in which no deaths occurred in consequence of the operation itself. The subsequent histories of only 2 out of the 10 cases are known. Death occurred in the 2 cases within two years from the date of the operation. The percentage of permanent cures, therefore, amounts to zero, since no patient recovered so as to be free from the disease for a period of three years. It is to be regretted that nothing is known of the 8 cases, since among the list there may be some cases of permanent cures. It is unfortunate that these cases have been lost sight of, since no statistics of permanent cure can be recorded unless the result is known. Gross reports 91 cases operated upon, of which 12 were permanently cured, giving 13 per cent. of permanent cures.

The writer reports 6 cases of sarcoma of the breast in which no death occurred in consequence of the operation itself. The subsequent histories are all known. Four of the six cases were permanently cured and the remaining 2 cases died from a return of the disease. This gives 66⅔ per cent. of permanent cures in sarcoma of the breast.

If the few suggestions which the writer has ventured to make will induce the members of the American Surgical Association to be on the alert for the early recognition of malignant disease and to employ a radical operation for its relief, and a repeated one if necessary, he will be more than repaid for the tedious labor involved in gathering together the clinical histories and the microscopical examination of this series of cases of malignant disease cured beyond the three years' limit of time.

Finally, the writer is a strong believer in the doctrine that all tumors, whether benign or malignant, should be removed. Benign tumors should be extirpated because a certain proportion of them undoubtedly degenerate into malignant tumors at special crises or periods of life. This is most apt to occur at a time when physiological atrophy takes place in an organ, as in the female breast, during the menopause. Another reason why supposed benign tumors should be excised is that certain malignant tumors remain quiescent for many years, and for this reason give rise to the belief that they are innocent growths, when in reality they are latent malignant neoplasms. The danger of leaving a supposed benign tumor becomes evident when it is considered that only a small minority of tumors in general are harmless.

Gross collected 649 cases of tumors of the breast, of which 587 were malignant and only 62 innocent. It follows, therefore, that the mere presence of a tumor in the body, especially in the breast, argues in favor of its malignancy, and for that reason the growth should not be permitted to remain. There is no benign tumor in which it has not been demonstrated that it may assume malignancy under favorable conditions.